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Gene-by-Environment Interactions on Alcohol Use Among Asian American College Freshmen

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ABSTRACT. Objective: Among northeast Asians, the variant aldehyde dehydrogenase allele, *ALDH2*2* (rs671, A/G, minor/major), has been inversely associated with alcohol dependence. The strength of the associations between *ALDH2*2* and drinking behaviors depends on the developmental stage, the phenotype studied, and other moderating variables. This study examined *ALDH2* gene status as a moderator of the associations between parental drinking, peer drinking, and acculturation with alcohol use among 222 Chinese American and Korean American college freshmen. **Method:** Negative binomial regressions were used to test the main and interactive effects of *ALDH2* with contextual factors on alcohol frequency (drinking days) and quantity (drinks per drinking day) in the past 3 months. **Results:** *ALDH2*2* was associated with more subjective flushing symptoms and longer length of flushing but was unrelated to both alcohol frequency and quantity. Peer drinking was positively associated with both alcohol frequency and quantity, but neither was moderated by *ALDH2.* We observed a nonsignificant trend for the interaction between parental drinking and *ALDH2* on alcohol frequency, where parental drinking was positively associated with alcohol frequency only among participants with *ALDH2*2.* We found a significant interaction between acculturation and *ALDH2* on alcohol frequency, where acculturation was positively associated with alcohol frequency only among those with *ALDH2*2.* Exploratory analyses stratified by Asian ethnic subgroup indicated that this interaction was driven primarily by the Korean subsample. **Conclusions:** Parental drinking and acculturation may facilitate more frequent drinking among those who have more intense reactions to alcohol (i.e., those with *ALDH2*2*) during the transition from high school to college. (*J. Stud. Alcohol Drugs, 78,* 531–539, 2017)

AS A GROUP, ASIAN AMERICANS report lower rates of substance use relative to other racial/ethnic groups in the United States (Substance Abuse and Mental Health Services Administration, 2014). However, substantial heterogeneity in rates of substance use and related problems exists among Asian ethnic subgroups (Choi, 2008; Harachi et al., 2001; Lum et al., 2009; Price et al., 2002; Wong et al., 2004). Rates of drinking among Asian Americans have increased over time and are especially high among Asian American college students (Grant et al., 2004; So & Wong, 2006). The transition from high school to college is particularly crucial because of decreased parental supervision, greater contact with drinking peers, and increased access to alcohol in college (Arnett, 2005; Simons-Morton et al., 2016). The identification of both psychosocial and genetic factors associated with alcohol use among college freshmen has important implications for targeted prevention and intervention efforts (Borsari et al., 2007).

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ALDH2 *Gene status and drinking among East Asians*

Variation in the aldehyde dehydrogenase gene, *ALDH2*2* (rs671), is present among approximately 30%–50% of individuals with northeast Asian origin, about 540 million individuals worldwide (Brooks et al., 2009; Eng et al., 2007; Li et al., 2009). Meta-analytic data indicate that individuals with one or two *ALDH2*2* allele(s) are four to nine times less likely to have alcohol dependence, and these associations were moderated by Asian ethnic subgroup, diagnostic criteria, and recruitment strategy (Luczak et al., 2006). The mechanistic pathway by which *ALDH2*2* is thought to lead to lower rates of alcohol use disorder is through reduced drinking due to the accumulation of acetaldehyde during alcohol metabolism (Eriksson, 2001; Wall, 2005), resulting in heightened and adverse physiological reactions to alcohol (also known as the alcohol flushing response; Brooks et al., 2009). Although *ALDH2*2* has a large effect size with alcohol dependence (Wall, 2005), it does not explain all variance in drinking because other genetic and psychosocial correlates are also crucial (Hendershot et al., 2005, 2009).

A recent review suggests that the associations between *ALDH2*2* and alcohol phenotypes vary across development (Wall et al., 2016). Except in one study of adolescent Korean adoptees (Irons et al., 2007), inverse associations between *ALDH2*2* with drinking behaviors were not observed in early adolescence (Irons et al., 2012) or during the first year of college (Hendershot et al., 2005; Luczak et al., 2014). The lack of a main effect of *ALDH2*2* with a composite measure

of drinking also was replicated in a recent study of young adult drinkers recruited from the community (Bujarski et al., 2015). The absence of an *ALDH2*2* main effect on alcohol phenotypes in younger samples does not preclude possible interactive effects with environmental risk factors, as the protective effects of *ALDH2*2* on drinking may be amplified in the context of high environmental risk. Alternatively, exposure to environmental risk factors may facilitate individuals with *ALDH2*2* to drink more despite the competing genetic protection against alcohol dependence.

Parental drinking, peer drinking, and acculturation

Parental, peer, and cultural factors account for racial/ethnic differences in substance use (Shih et al., 2010; Thai et al., 2010) and are key constructs in ecological models of substance use among Asian American youth (Harachi et al., 2001; Hong et al., 2011). Parental drinking is a risk factor for drinking behaviors that is both genetically and environmentally mediated, such as through overt modeling and parenting behaviors (Chassin et al., 1993; Latendresse et al., 2008; White et al., 2000). Although parental influence on drinking is strongest during adolescence, such influence could extend into the college years (Wood et al., 2004). Among college students, the associations between retrospective parenting behaviors and alcohol-related problems were significant among European American but not Asian American college students (Luk et al., 2015). Two recent studies showed that the association between parental drinking and drinking among Asian American youth was moderated by *ALDH2* status (Bujarski et al., 2015; Irons et al., 2012), but these studies did not disaggregate the effects on alcohol frequency versus quantity.

Relative to parental influence, peer influences on drinking through both socialization and selection effects are often stronger and more robust (Kim et al., 2002; Kiuru et al., 2010; Simons-Morton, 2007; Windle, 2000). Affiliation with peers who often drink is one of the strongest correlates of drinking behaviors during the transition into young adulthood (Simons-Morton et al., 2016). Peer influences on college drinking may operate through mechanisms such as peer modeling, drinking norms, and overt offers of alcoholic drinks (Borsari & Carey, 2001). Prior research indicated that genetic contributions to alcohol use become stronger as deviant peer affiliation or peer drinking increased (Dick et al., 2007; Guo et al., 2009; Kendler et al., 2011), supporting the importance of testing Genetic × Peer interactions on drinking behaviors.

Acculturation to the American culture is a risk factor for drinking behaviors among most Asian American youth (Hahm et al., 2003; Luk et al., 2013; Price et al., 2002). However, when disaggregated across Asian ethnic subgroups, acculturation may be unrelated to or even become a risk factor for drinking among Korean American college students (Cook et al., 2009; Hendershot et al., 2008). Because the effect of acculturation on drinking often reflects the disparate drinking rates between the country of origin and those in the United States, these findings may be understood in the context of low drinking rates in China and Taiwan compared with high drinking rates in South Korea, which approximate or exceed the drinking levels in the United States (Helzer et al., 1990; Weatherspoon et al., 1994). Importantly, cultural factors could facilitate drinking among individuals with *ALDH2*2* despite the alcohol flushing response (Brooks et al., 2009; Li & Rosenblood, 1994). The *ALDH2* × Acculturation interaction on drinking was rarely tested. In one prior study of young adult drinkers, this interaction was not significant (Bujarski et al. 2015).

Current study

The current study examined *ALDH2* gene status as a moderator of the associations between parental drinking, peer drinking, and acculturation with alcohol use. In a sample of 222 Chinese American and Korean American college freshmen, we first examined whether *ALDH2* gene status was associated with subjective flushing symptoms, length of flushing, alcohol frequency, and alcohol quantity. We then tested the main and interactive effects of *ALDH2* gene status, parental drinking, peer drinking, and acculturation on alcohol frequency and quantity. We hypothesized that *ALDH2*2* would be positively associated with subjective flushing symptoms and length of flushing, but inversely associated with alcohol frequency and quantity. We further hypothesized that *ALDH2*2* would moderate the associations between parental drinking, peer drinking, and acculturation with alcohol frequency and quantity.

Method

Sample and procedures

Data were collected from 305 Chinese American and Korean American college freshmen (M_{age} = 18.7 years, *SD* = 0.7; 50% female; 50% Korean) enrolled at the University of California, San Diego. These two Asian ethnic subgroups were specifically chosen because they both have a high prevalence of *ALDH2*2* and exhibit differences in alcohol use disorder in epidemiological studies. Because the effect of *ALDH2*2* is theorized to be contingent upon prior experience with alcohol, we restricted the analytic sample to lifetime drinkers only (n = 222), defined as those who reported ever, even once, having a drink (not a sip or two) of any type of alcoholic beverage.

Participants were recruited via advertisements posted on the university online system and flyers posted on campus. Potential participants were screened by telephone to ensure they were a freshman student between ages 18 and 20 years

and both parents were entirely of either Chinese or Korean descent. Eligible participants completed both interviews with a trained research assistant and self-report measures on computers in the laboratory. Blood samples were obtained via fingertip puncture to determine *ALDH2* genotype status (Hendershot et al., 2009). The entire assessment was about 2.5 hours long. Participants were compensated $100 for their participation. All study procedures were approved by the university's Institutional Review Board.

Measures

ALDH2 *gene status.* The distribution of participants with *ALDH2*1/*1* (GG), *ALDH2*2/*1* (AG), and *ALDH2*2/*2* (AA) were as follows: 133 (59.9%), 81 (36.5%), and 8 (3.6%). Because of the small number of participants with *ALDH2*2/*2,* they were combined with participants with *ALDH2*1/*2,* resulting in two groups: individuals without *ALDH2*2* labeled as "*ALDH2*2*(−)", and individuals with one or two *ALDH2*2* allele(s) labeled as "*ALDH2*2*(+)".

Alcohol flushing. Participants were asked (yes/no) whether they experience 17 different flushing symptoms (e.g., "my face turns pink or red," "my heart beats faster," "I get dizzy," "I perspire," and "I feel pounding in my head") after they drink alcohol. The sum of these 17 items was used to represent subjective flushing symptoms. Length of flushing was assessed using an item inquiring about the number of minutes flushing usually lasts. Participants were instructed to enter 0 if they do not experience flushing.

Parental drinking. Participants were asked (yes/no) whether their mothers and fathers engaged in past regular drinking, past occasional drunkenness, current regular drinking, and current occasional drunkenness. Each drinking behavior was coded as 1 if participants indicated that either parent or both parents were engaged in that drinking behavior. The sum of these four drinking behaviors was used to represent parental drinking. The Cronbach's α for this scale was .78 for the entire sample, .77 for *ALDH2*2*(−) participants, and .80 for *ALDH2*2*(+) participants.

Peer drinking. Participants responded to four questions on alcohol use involvement by close friends in the past 3 months. They were asked how many of their close friends drink beer, wine, or distilled spirits at least occasionally or regularly. They were also asked how many of their close friends get drunk at least occasionally or regularly. Response options ranged from 0 (*none*) to 5 (*all*). We took the mean of these items. The Cronbach's α for this scale was .93 for the entire sample, .93 for *ALDH2*2*(−) participants, and .92 for *ALDH2*2*(+) participants.

Acculturation. The original 21-item Suinn–Lew Asian Self-Identity Acculturation Scale (Suinn et al., 1992) was used to assess participants' cultural origins and identity, language, media, and food preferences, as well as heritage, pride, and values. Response options were on a Likert scale ranging from 1 to 5, with a higher score reflecting higher levels of acculturation. The mean of these items was used to represent acculturation. The Cronbach's α for this scale was .85 for the entire sample, .84 for *ALDH2*2*(−) participants, and .85 for *ALDH2*2*(+) participants.

Alcohol use. Alcohol use frequency was measured by a single item: "Over the last 3 months, on average, how many days a month did you drink?" Alcohol quantity was measured by a single item: "On the days that you drank during the past 3 months, how many standard drinks did you usually have each day?" A standard drink was defined as 12 ounces of beer, 1 shot of distilled spirits (1.5 ounces either straight or in a mixed drink), or 5 ounces of wine.

Data analysis

Descriptive statistics were conducted to understand sample characteristics for the full sample and by *ALDH2.* To examine the unadjusted associations, *t* tests were used to compare mean differences in subjective flushing symptoms and length of flushing by *ALDH2.* Negative binomial regressions were used to compare rates of alcohol use frequency and quantity by *ALDH2* and to account for nonnormal distributions of these outcomes. To examine the adjusted associations and interaction effects, two separate multivariate negative binomial regressions were used to model alcohol frequency and alcohol quantity. Sex and Asian ethnic subgroup were included as covariates. All three continuous predictors were centered. Interaction terms were created using centered continuous predictors and dichotomous *ALDH2* status. Model building followed two steps. In preliminary models, each predictor (parental drinking, peer drinking, and acculturation) and its interaction with *ALDH2* were first tested with the additional *ALDH2* × Covariate interactions (i.e., *ALDH2* × Sex and *ALDH2* × Ethnicity) included in the same model (Keller, 2014). Because all *ALDH2* × Covariate interactions were not significant, they were trimmed from the final full model in which all three predictors and their interactions with *ALDH2* were included in the same model. We probed significant interactions using simple slope analyses following Aiken and West (1991). All analyses were conducted in Stata 14 (StataCorp LP, College Station, TX).

Results

Descriptive statistics

Sample characteristics are presented in Table 1. There were no significant differences between *ALDH2*2*(+) and *ALDH2*2*(−) participants. The allele frequencies for *ALDH2*2*(+) were 55.1% (n = 49) among Chinese and 44.9% (n = 40) among Koreans (p = .09). Bivariate correlations by *ALDH2* status are presented in Table 2. Parental drinking was positively associated with alcohol frequency

Table 1. Sample characteristics for the full sample and by *ALDH2* gene status

	Full sample (n = 222)		*ALDH2*2*(−) (n = 133)		*ALDH2*2*(+) (n = 89)			
Variable	*M* or (*n*)	*SD* or (%)	*M* or (*n*)	*SD* or (%)	*M* or (*n*)	*SD* or (%)	*t* or (χ^2)	*p*
Demographics								
Age	18.68	0.70	18.68	0.69	18.67	0.72	0.03	.98
Sex								
Female	(105)	(47.30%)	(60)	(45.11%)	(45)	(50.56%)	(0.64)	.43
Male	(117)	(52.70%)	(73)	(54.89%)	(44)	(49.44%)		
Ethnicity								
Korean	(107)	(51.80%)	(75)	(56.39%)	(40)	(44.94%)	(2.80)	.09
Chinese	(115)	(48.20%)	(58)	(43.61%)	(49)	(55.06%)		
Predictors								
Parental drinking	1.27	1.43	1.33	1.43	1.17	1.42	0.83	.41
Peer drinking	1.96	1.15	1.90	1.18	2.04	1.10	-0.92	.36
Acculturation	2.93	0.45	2.92	0.45	2.95	0.45	-0.39	.69
Outcomes								
Alcohol frequency	3.03	3.31	3.02	3.13	3.03	3.59	-0.03	.98
Alcohol quantity	3.79	3.15	3.98	3.17	3.52	3.12	1.07	.29

Notes: Ethnicity refers to Asian ethnic subgroups. Means and standard deviations are presented for continuous variables. Frequencies and percentages are presented for categorical variables. Differences in demographics, predictors, and outcomes were evaluated using *t* tests for continuous variables and chi-square tests for categorical variables. Alcohol frequency reflects number of drinking days per month. Alcohol quantity reflects number of drinks per drinking day.

among *ALDH2*2*(+) participants only. Peer drinking was positively associated with alcohol frequency and quantity regardless of *ALDH2* status. Acculturation was positively associated with alcohol frequency and quantity only among *ALDH2*2*(+) participants.

Unadjusted associations between ALDH2, alcohol flushing, and alcohol use

Subjective flushing symptoms were higher among *ALDH2*2*(+) participants (M = 6.71, SD = 3.66) compared with *ALDH2*2*(−) participants (M = 3.35, SD = 2.38), $t(220) = 8.30$, $p < .001$. The length of flushing in minutes was also higher among *ALDH2*2*(+) participants (M = 55.45, SD = 61.05) compared with *ALDH2*2*(−) participants (M = 12.68, SD = 23.79), $t(220) = 7.30$, $p < .001$. However, *ALDH2*2*(+) participants did not report decreased alcohol frequency (b < 0.01, SE = 0.14, IRR [incidence risk ratio] = 1.00, p = .98) or alcohol quantity (b = -0.12, SE = 0.12, IRR = 0.88, p = .29) compared with *ALDH2*2*(−) participants.

Moderation analyses by ALDH2 gene status

Results from negative binomial regression models are presented in Table 3 and are illustrated in Figure 1. In the first model, there was a significant main effect of peer drinking on alcohol frequency, and a significant interaction between acculturation and *ALDH2* on alcohol frequency. Simple slope analyses indicated that acculturation was positively associated with alcohol frequency among *ALDH2*2*(+) participants (b = 0.94, SE = 0.23, IRR = 2.57, $p < .001$) but was unrelated to alcohol frequency among *ALDH2*2*(−) participants (b = -0.02, SE = 0.17, IRR = 0.98, p = .89). The interaction between parental drinking and *ALDH2* status exhibited a nonsignificant trend, such that parental drinking was positively associated with alcohol use frequency among *ALDH2*2*(+) participants (b = 0.17, SE = 0.07, IRR = 1.18, p = .003), but was unrelated to alcohol frequency among *ALDH2*2*(−) participants (b = 0.02, SE = 0.06, IRR = 1.02, p = .73). In the second model, there was similarly a significant main effect of peer drinking on alcohol quantity, but none of the interactions on alcohol quantity were significant. As shown by the 95% confidence interval error bars in Figure 1, the effects of *ALDH2*2* on alcohol frequency and quantity were not significant at the mean or 1 *SD* above or below the mean of any predictor.

Exploratory analyses with stratification by Asian ethnic group

Because acculturation was differentially associated with alcohol use among Korean Americans versus Chinese Americans in a college sample (Hendershot et al., 2008), stratified analyses were conducted to further unpack whether the interaction between acculturation and *ALDH2* on alcohol frequency would be observed in only one or both groups. As illustrated in Figure 2, the *ALDH2* × Acculturation interaction was significant among Koreans (b = 1.32, SE = 0.47, IRR = 3.73, p = .006; Figure 2a) but not among Chinese (b = 0.56, SE = 0.41, IRR = 1.75, p =.17; Figure 2b). Among Koreans only, acculturation was positively associated with alcohol frequency among *ALDH2*2*(+) participants (b = 0.94, SE = 0.41, IRR = 2.56, p = .02) and was unrelated to alcohol frequency among *ALDH2*2*(−) participants (b = -0.38, SE = 0.24, IRR = 0.69, p = .11). Postestimation of marginal effects showed that the effect of *ALDH2* on alcohol frequency

Table 2. Bivariate correlations by *ALDH2* gene status

	*ALDH2*2*(−) (*n* = 133)						
Variable	1.	2.	3.	4.	5.	6.	7.
1. Sex female	1.000						
2. Korean ethnicity	-.025	1.000					
3. Parental drinking	.033	.023	1.000				
4. Peer drinking	-.007	-.020	.122	1.000			
5. Acculturation	-.164	.009	-.019	.119	1.000		
6. Alcohol frequency	-.100	-.086	.027	**.448**	.083	1.000	
7. Alcohol quantity	-.166	.032	.142	**.390**	-.004	**.431**	1.000
	*ALDH2*2*(+) (*n* = 89)						
Variable	1.	2.	3.	4.	5.	6.	7.
1. Sex female	1.000						
2. Korean ethnicity	-.191	1.000					
3. Parental drinking	-.073	.052	1.000				
4. Peer drinking	.005	**.261**	.123	1.000			
5. Acculturation	**-.221**	.119	.105	.190	1.000		
6. Alcohol frequency	-.154	.143	**.277**	**.326**	**.389**	1.000	
7. Alcohol quantity	**-.328**	.083	.136	**.305**	**.252**	**.660**	1.000

Notes: Ethnicity refers to Asian ethnic subgroups. Bivariate correlations for participants with *ALDH2*2*(−) are presented in the top part of this table. Bivariate correlations for participants with *ALDH2*2*(+) are presented in the bottom part of this table. All $p < .05$ are highlighted in **bold.**

was not significant at the mean ($p = .12$) or 1 *SD* above ($p = 1.00$) or below the mean ($p = .14$). The *ALDH2* × Asian Ethnic Subgroup × Acculturation three-way interaction on alcohol frequency was not significant ($b = 0.82$, $SE = 0.63$, IRR = 2.27, $p = .19$).

Discussion

The transition into college is marked by increased environmental exposure to drinking risks. In this study, we tested whether the associations between well-established risk factors in the family, peer, and cultural domains and alcohol frequency and quantity were moderated by *ALDH2* gene status in a sample of Chinese American and Korean American college freshmen. Consistent with prior research, *ALDH2*2* was associated with more subjective flushing symptoms and longer length of flushing response. Contrary to our hypothesis, *ALDH2* status was not associated with frequency or quantity of drinking, replicating findings from two prior studies among college freshmen (Hendershot et al., 2005; Luczak et al., 2014). Collectively, these prior studies and our current results suggest that the protective effect of *ALDH2*2* on drinking behavior emerges later in development following more experience with alcohol (Wall et al., 2016) and that Asian American college freshmen with and without *ALDH2*2* engaged in similar levels of drinking behaviors despite those with *ALDH2*2* reporting heighted and adverse physiological reactions to drinking alcohol.

To our knowledge, a significant interaction between acculturation and *ALDH2*2* status with drinking among Asian Americans has not been documented in previous literature. Prior conceptualizations of the influence of acculturation on alcohol use have largely focused on the degree to which drinking levels differ across the culture in the country of origin and in the United States (Hendershot et al., 2008; Price et al., 2002). Psychosocial factors such as parental attachment (Hahm et al., 2003) and religiosity (Luk et al., 2013) have been shown to buffer against the adverse effect of acculturation on alcohol use among Asian Americans. However, genetic data were often unavailable in prior studies, which prohibited tests of interaction with *ALDH2* status. We extended these studies by demonstrating that accul-

Table 3. Negative binomial regression models on alcohol frequency and alcohol quantity (*n* = 222)

	Alcohol frequency				Alcohol quantity			
Variable	*b*	*SE*	IRR	*p*	*b*	*SE*	IRR	*p*
Sex female	-0.01	0.13	0.98	.882	**-0.42**	**0.10**	**0.66**	**<.001**
Ethnicity Korean	-0.04	0.13	0.97	.784	0.01	0.10	1.01	.898
*ALDH2*2*	-0.12	0.15	0.89	.419	-0.13	0.12	0.88	.288
Parental drinking	0.02	0.06	1.02	.732	0.08	0.05	1.08	.084
Peer drinking	**0.41**	**0.07**	**1.50**	**<.001**	**0.30**	**0.06**	**1.35**	**<.001**
Acculturation	-0.02	0.17	0.98	.886	-0.10	0.14	0.91	.506
Parental drinking × *ALDH2*	0.15	0.09	1.16	.088	-0.03	0.07	0.97	.706
Peer drinking × *ALDH2*	-0.11	0.12	0.90	.370	-0.05	0.10	0.95	.637
Acculturation × *ALDH2*	**0.97**	**0.29**	**2.63**	**.001**	0.41	0.23	1.50	.082

Notes: Ethnicity refers to Asian ethnic subgroups. IRR = Incidence risk ratio. All $p < .05$ are highlighted in **bold.**

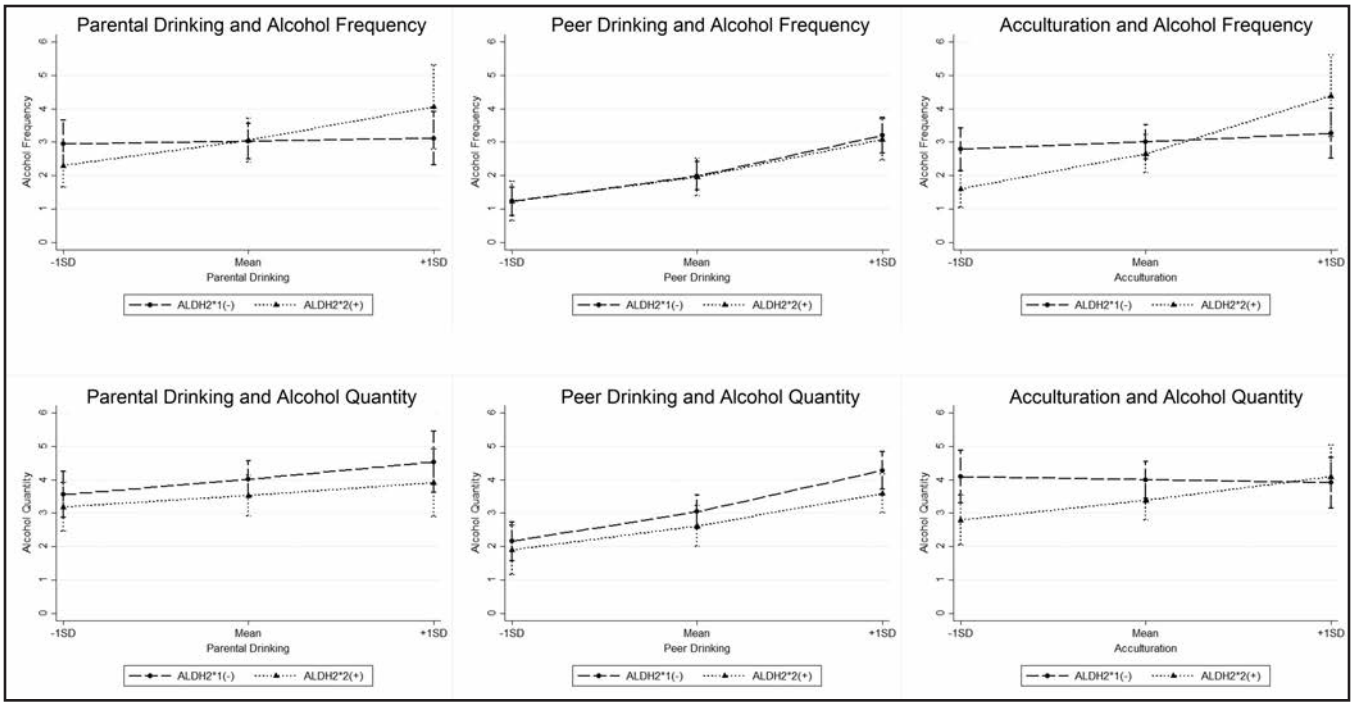

FIGURE 1. Parental drinking, peer drinking, and acculturation as correlates of alcohol frequency and quantity by *ALDH2* gene status

turation was a risk factor for alcohol frequency only among those with *ALDH2*2* in our full analytic sample. Individuals with *ALDH2*2* may experience competing genetic and environmental influences, such that relative to those without *ALDH2*2,* they tend to be more sensitive to cultural influences that may lead them to drink more frequently despite the *ALDH2*2* genetic protection. In analyses stratified by Asian ethnic subgroup, we further found that this Gene × Acculturation interaction was driven by the Korean American participants, possibly reflective of the relatively higher drinking frequency among Korean Americans without an *ALDH2*2* allele. These Asian ethnic subgroup differences provide further insight into why acculturation may not be a risk factor for drinking behaviors among Korean American youth (Cook et al., 2009; Hendershot et al., 2008).

The nonsignificant parental drinking by *ALDH2* interaction trend exhibited a pattern similar to the interaction between acculturation and *ALDH2,* in which parental drinking was associated with increased alcohol frequency only among those with *ALDH2*2.* Our findings are somewhat in line with prior studies showing the presence of a parental drinking variable by *ALDH2* gene status interaction on alcohol use (Bujarski et al., 2015; Irons et al., 2012), even though the interaction patterns were not entirely consistent across studies. In our study, the *ALDH2*2* effect on alcohol frequency was not significant at varying levels (mean, 1 *SD* above or below the mean) of parental drinking. However, we found that environmental risk was amplified only among participants with *ALDH2*2,* who in theory are protected from alcohol use risk. It is possible that parental drinking facilitated more frequent drinking among individuals who tend to have stronger physiological reactions to alcohol, which in part may be attributable to the socialization or modeling influences by parents.

Peer drinking emerged as the sole consistent predictor of both alcohol frequency and quantity. Contrary to prior studies showing significant Gene × Peer Variable interactions on alcohol use (Dick et al., 2007; Guo et al., 2009; Kendler et al., 2011), we did not find significant interaction effects between peer drinking and *ALDH2* gene status on alcohol use among Asian Americans. Our peer drinking main effect replicated a large body of literature suggesting that affiliation with friends who drink is one of the strongest correlates of adolescent and young adult drinking (Kiuru et al., 2010; Simons-Morton, 2007; Simons-Morton et al., 2016; Windle, 2000). Indeed, vulnerability to negative peer influence may be a key underlying mechanism by which distal protective and risk factors in the family and school domains are indirectly associated with substance use risk among Asian American youth (Kim et al., 2002). Because of the cross-sectional nature of this study, we did not test peer drinking as a mediator of the associations between distal predictors and drinking behaviors. Nonetheless, the consistency and magnitude of the associations between peer drinking and alcohol use variables are noteworthy and generally support peer context as a universal prevention and intervention target for underage drinking among Asian American college freshmen.

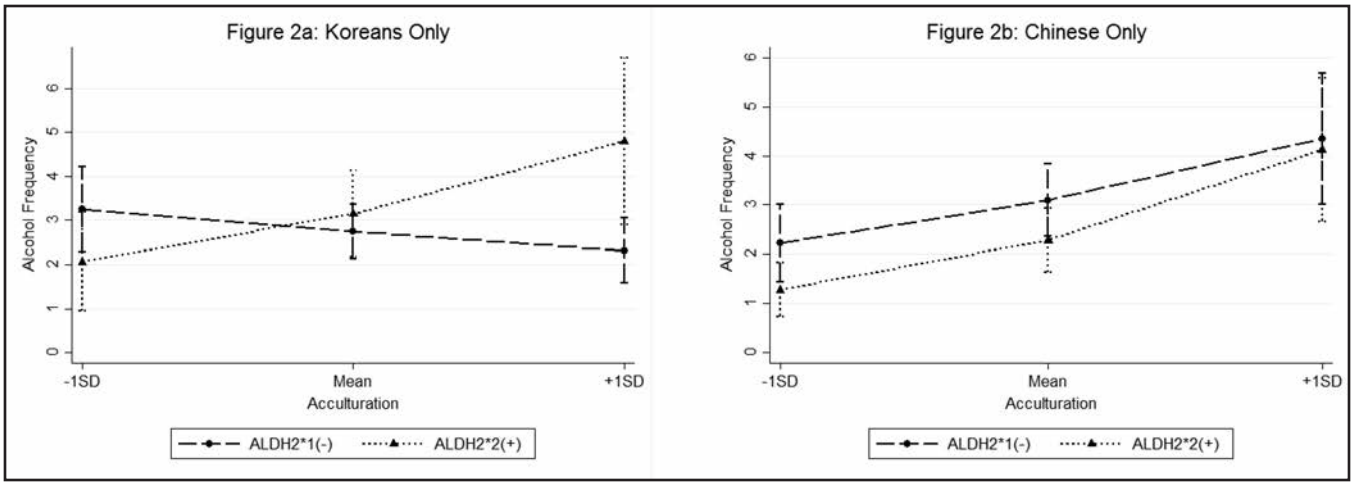

FIGURE 2. Acculturation × *ALDH2* interaction on alcohol frequency among Korean Americans (n = 107) and Chinese Americans (n = 115). *Note:* Acculturation was a risk factor for increased alcohol frequency among Chinese Americans regardless of *ALDH2* status. Korean Americans with *ALDH2*2* and a high level of acculturation were at elevated risk for more frequent drinking.

The current findings have important clinical implications. Considerable research indicates that individuals with *ALDH2*2* are less likely to develop alcohol-related problems and alcohol use disorder across development (Luczak et al., 2006, 2014). However, individuals who engage in drinking despite possession of *ALDH2*2* tend to have greater odds of developing alcohol-related cancers, including esophageal cancer, as well as head and neck cancers (Brooks et al., 2009; Hendershot, 2011; Lewis & Smith, 2005). These findings have prompted researchers to develop genetic feedback interventions for reducing alcohol-related health risks attributed to *ALDH2* (Hendershot et al., 2010). Our findings indicate that individuals with *ALDH2*2* may engage in more frequent drinking as a function of parental drinking and acculturation, highlighting the potential benefit of augmenting genetic feedback interventions with family-oriented and/or culturally specific feedback to optimize the efficacy of alcohol prevention and intervention programs for Asian college students.

This study has several limitations. First, the data are cross-sectional, so the direction of effects cannot be determined. For example, participants' drinking may influence peer drinking the same way peer drinking may facilitate participants' drinking. Prospective research is needed to test the temporal sequence of developmental risk and protective factors as well as the emergence of alcohol use and problems among Asian American youth over time. Second, measurement of Asian ethnic subgroup, parental drinking, peer drinking, and acculturation all relied on participants' report, which may be susceptible to bias. For example, participants may not fully know the extent to which their parents engaged in drinking, and so their estimation of parental drinking could be biased. Third, as a first step to explore Gene × Environment interactions on alcohol use, we focused on *ALDH2* status and did not consider other genetic factors such as variation in the alcohol dehydrogenase (*ADH*) genes, which are also important in the etiology of drinking among Asians (Wall et al., 2016).

Despite these limitations, the current study is the first to demonstrate a significant interaction between acculturation and *ALDH2* gene status on alcohol frequency in a sample of Asian American college freshmen. Specifically, Korean American college freshmen with *ALDH2*2* may drink more often, but not more drinks, as a function of the degree to which they adapt to the American culture. As *ALDH2* gene status has been shown to modify the associations between alcohol consumption and alcohol-related problems over time (Luczak et al., 2014), prospective research is warranted to determine if these *ALDH2* × Environment interactions are significant initiators of mechanistic pathways that lead to the development of more severe alcohol-related problems among Asian Americans.

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